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Application No.	:	**2,437,468**
Owner	:	ONCOLYTICS BIOTECH INC.
Title	:	**SENSITIZATION OF CHEMOTHERAPEUTIC AGENT RESISTANT NEOPLASTIC CELLS WITH REOVIRUS**
Classification	:	A61K-35/76
Your File No.	:	**15157-2-N.P.**
Examiner	:	C Brewer

YOU ARE HEREBY NOTIFIED OF :

- A REQUISITION BY THE EXAMINER IN ACCORDANCE WITH SUBSECTION 30(2) OF THE *PATENT RULES*;
- A REQUISITION BY THE EXAMINER IN ACCORDANCE WITH SECTION 29 OF THE *PATENT RULES*.

IN ORDER TO AVOID **MULTIPLE ABANDONMENTS** UNDER PARAGRAPH 73(1)(A) OF THE *PATENT ACT*, A WRITTEN REPLY **TO EACH REQUISITION** MUST BE RECEIVED WITHIN **6** MONTHS AFTER THE ABOVE DATE.

Applicant's letter of July 22, 2005 has been received and the application has been examined having regard to applicant's arguments. However, the examiner considers that the application still does not comply with the *Patent Act* or *Rules*.

The number of claims in this application is 94.

References Re-Applied:

Canadian Patent Applications

2,283,280	filed 12-08-1998; laid open 25-02-1999	Coffey et al.
2,360,833	filed 18-02-2000; laid open 31-08-2000	Coffey et al.

The references of Coffey et al. independently disclose the use of reovirus in the treatment of neoplasms, neoplastic cells, and cell proliferative disorders. In addition, these references disclose the option of combining said reovirus use with chemotherapeutic agents.

Publication

Bryson and Cox (1988) Cancer Immunol Immunother 26(2):132-138.

Bryson and Cox disclose the use of reovirus in combination with a chemotherapeutic agent, namely, BCNU to treat neoplastic cells. In addition, the authors disclose that BCNU when administered alone was ineffective as a treatment. However, BCNU administration in combination with reovirus administration provided a therapeutic effect.

The examiner has identified the following defects in the application:

Claims 1 to 11, 31, 33, 35 to 43, 57, 59, 61 to 71, 91, and 93 do not comply with paragraph 28.2(1)(*a*) of the *Patent Act*. The subject-matter defined by these claims was disclosed independently in the above references by Coffey et al. more than one year before the filing date of the present patent application. In the correspondence dated July 22, 2005 applicant asserts that the references of Coffey et al. "*fail to teach the sensitization of neoplastic cells to chemotherapeutic agent, particularly an increase in sensitivity of at least 20%*". Nevertheless, these prior art documents are prejudicial to the novelty of these claims as they disclose the use of reovirus in combination with a chemotherapeutic agent to treat neoplastic cells. The included recitation does not correspond to a distinguishing limitation as alleged by the applicant. Rather, the sensitization referred to appears to be the discovery of a functional consequence of the combined use and not a new and patentably distinct combination to treat neoplastic cells. Notably, the therapeutic result regardless of the claim language is the same, namely, the treatment of neoplastic cells. Accordingly, the objection is maintained.

Claims 12 to 25, 31, 33, 44 to 53, 57, 59, 72 to 85, 91, and 93 do not comply with paragraph 28.2(1)(*b*) of the *Patent Act* because these claims include subject matter disclosed in Bryson and Cox before the claim date. In particular, Bryson and Cox disclose that combined therapy with reovirus and BCNU lead to a significantly greater survival level than animals treated with BCNU or reovirus alone. Moreover, the dosage of BCNU when used alone had no therapeutic effect. Given that applicant has defined the word "sensitizing" on page 13 of the instant description to read: "*the act of enhancing the sensitivity of a neoplastic cell to a chemotherapeutic agent*". It is clear that the prior disclosure of Bryson and Cox fits this definition and this prior art document inherently anticipates these claims. Further, the data presented by Bryson and Cox demonstrate that neoplastic cells were present which were refractory to the BCNU. Furthermore, the mere recitation of "*increase in sensitivity to the chemotherapeutic agent is at least 20%*" in these claims does not distinguish the use, pharmaceutical composition, and package for a certain use from this prior disclosure. As noted above, the alleged effect is considered to be a functional consequence of the combined use and not a new patentably distinct combination. Thus, the therapeutic benefit with the combined use is inherently anticipated by this prior art document. Accordingly, the objection is maintained.

Claims 26 to 29, 54 to 56, and 86 to 90 do not comply with section 84 of the *Patent Rules*. The description fails to provide support for the utility of reovirus to prevent neoplastic cells from developing drug resistance to a chemotherapeutic agent. In example 1, applicant has demonstrated that cisplatin alone does not reduce tumor growth. However, when cisplatin is administered in combination with reovirus a reduction in tumor growth is observed which exceeds that observed when reovirus is administered alone. This factual support does not lead to the conclusion that the subject matter of these claims would have the predicted utility. It is well recognized in the art that drug resistance is very complex and unpredictable. Despite

applicant's assertion that an initial treatment with a chemotherapeutic agent in conjunction with reovirus would prevent drug resistance, applicant has not provided sufficient evidence to support the position that reovirus has the alleged capability (Apotex Inc. v. Wellcome Foundation., [2002] 4 S.C.R. 153 or 21 C.P.R. (4th) 499). Accordingly, the objection is maintained.

Claims 31 to 34, 57 to 60, 91 to 94 are broader in scope than the teaching of the description. To comply with section 84 of the *Patent Rules* the claims must specify that the virus is reovirus. The description does not draw adequate support for any additional viruses. Undue experimentation would be required by the skilled person to identify viruses which in combination with a chemotherapeutic agent would provide the alleged effect.

If the defects referred to in the requisition are not overcome, the application may be rejected in a FINAL ACTION.

In view of the foregoing defects, the applicant is requisitioned, under subsection 30(2) of the *Patent Rules*, to amend the application in order to comply with the *Patent Act* and the *Patent Rules* or to provide arguments as to why the application does comply.

Section 29 of the Patent Rules requisition

Under section 29 of the *Patent Rules*, the applicant is requisitioned to provide:

- identification of any prior art cited in respect of the United States Patent and Trademark Office, and European Patent Office applications describing the same invention on behalf of the applicant or on behalf of any other person claiming under an inventor named in the present application, and the patent numbers, if granted, subsequent to applicant's correspondence received on July 22, 2005 under paragraph 29(1)(*a*) of the *Patent Rules*.

To satisfy this requisition, applicant should provide all the preceding information or documents, or provide in accordance with subsection 29(3) of the *Patent Rules* a statement of reasons why any information or document is not available or known.

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